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Anti-CD8 Monoclonal Antibody Therapy Is Effective in the Prevention and Treatment of Experimental Autoimmune Glomerulonephritis.

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ABSTRACT. Experimental autoimmune glomerulonephritis (EAG), which is an animal model of Goodpasture's disease, can be induced in Wistar Kyoto rats by a single injection of rat glomerular basement membrane (GBM) in adjuvant. EAG is characterized by circulating and deposited anti-GBM antibodies, focal necrotizing glomerulonephritis with crescent formation, and glomerular infiltration by T cells and macrophages. Our hypothesis was that T cell-mediated immunity, in addition to humoral immunity, was necessary for the development of crescentic nephritis in this model. To investigate the role of CD8(+) T cells in the pathogenesis of EAG, the in vivo effects of an anti-CD8 monoclonal antibody (OX8) were examined, with administration starting at the time of immunization (prevention) or 2 wk after immunization, when glomerular abnormalities were first detected (treatment). When administered intraperitoneally at 5 mg/kg, three times per week, from week 0 to week 4 (prevention), OX8 completely inhibited the development of albuminuria, deposits of fibrin in the glomeruli, glomerular and interstitial abnormalities, the influx of CD8 (+) T cells and macrophages, and glomerular expression of granzyme B and inducible nitric oxide synthase. Circulating anti-GBM antibody levels were not reduced, but there was a reduction in the intensity of antibody deposition on the GBM. When administered at the same dose from week 2 to week 4 (treatment), OX8 greatly reduced the severity of EAG; in particular, the formation of crescents was prevented. These studies demonstrate that anti-CD8 monoclonal antibody therapy is effective in both the prevention and treatment of EAG. They confirm the importance of T cell-mediated immunity in the pathogenesis of this model of Goodpasture's disease.

Similar therapeutic approaches may be worth investigating in human crescentic glomerulonephritis.

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